



1600
\$

PATENT
ATTORNEY DOCKET NO. 50304/113001

Certificate of Mailing: Date of Deposit: April 6, 2007

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Megan Kiley

Printed name of person mailing correspondence

Megan Kiley
Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: WAER et al.

Confirmation No.: 3050

Serial No.: 10/595,126

Art Unit: 1626

§371 Date: 2/27/2006

Examiner: S. Young

Customer No.: 21559

Title: IMMUNOSUPPRESSIVE EFFECTS OF PTERIDINE DERIVATIVES

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Applicants submit the references listed on the enclosed Form PTO-1449, copies of which are enclosed, with the exception of U.S. patents and U.S. patent application publications. Included in the list are a communication from a foreign patent office in a counterpart application and copies of communications from a corresponding international application.

Submission of this statement is not a representation that a search has been made,

nor is the inclusion of information in this statement an admission that the information is material to patentability.

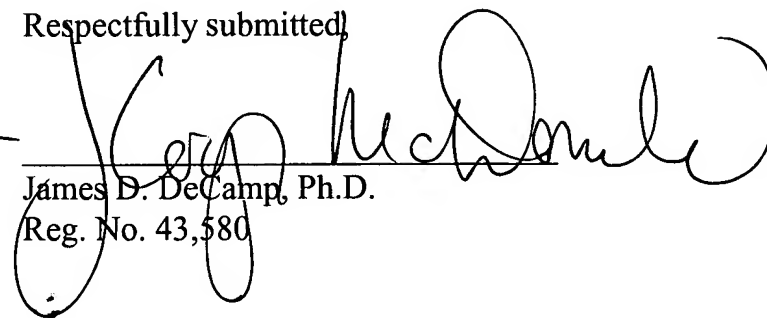
This statement is being filed after a first Office action on the merits, but before the mailing of a final Office action or a Notice of Allowance. A check for \$180.00 in payment of the late submission fee set forth in 37 C.F.R. § 1.17(p) is enclosed.

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Date. April 6, 2007

Respectfully submitted,

James D. DeCamp, Ph.D.
Reg. No. 43,580



Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045

| |
|--|
| J. Cooper McDonald, Ph.D. Reg. No. 52,011 |
|--|

Sheet 1 of 7

| | | |
|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | Attorney Docket No. | 50304/113001 |
| | Serial No. | 10/595,126 |
| | Applicant | WAER et al. |
| | Filing Date | February 27, 2006 |
| | Group | 1626 |
| | IDS Filed | April 6, 2007 |

| U.S. PATENT DOCUMENTS | | | | | | |
|-----------------------|-----------------|-------------------------|-----------------------|-------|----------|------------------------------|
| Examiner's Initials | Document Number | Publication/ Issue Date | Patentee or Applicant | Class | Subclass | Filing Date (If Appropriate) |
| | 2003/236255 | 12-25-2003 | Waer et al. | | | |
| | 2,512,572 | 06-20-1950 | Smith, Jr. et al. | | | |
| | 2,581,889 | 01-08-1952 | Timmis | | | |
| | 2,665,275 | 01-05-1954 | Campbell et al. | | | |
| | 2,667,486 | 01-26-1954 | Cain | | | |
| | 2,740,784 | 04-03-1956 | Sletzinger et al. | | | |
| | 2,940,972 | 06-14-1960 | Roch | | | |
| | 3,071,587 | 01-01-1963 | Curran | | | |
| | 3,081,230 | 03-12-1963 | Weinstock et al. | | | |
| | 3,159,628 | 12-01-1964 | Pachter et al. | | | |
| | 3,475,425 | 10-1969 | Roch, Joseph | | | |
| | 3,859,287 | 01-07-1975 | Parish et al. | | | |
| | 5,047,405 | 09-10-1991 | Gennari | | | |
| | 5,665,772 | 09-09-1997 | Cottens et al. | | | |
| | 5,780,462 | 07-14-1998 | Lee et al. | | | |
| | 5,843,943 | 12-1-1998 | Carson et al. | | | |
| | 5,929,046 | 07-27-1999 | McMurry et al. | | | |
| | 5,992,713 | 11-30-1999 | Manabat | | | |
| | 6,331,547 | 12-18-2001 | Zhu et al. | | | |
| | 6,440,991 | 08-27-2002 | Zhu et al. | | | |
| | 6,844,343 | 01-2005 | Pfleiderer et al. | | | |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | |
|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | Attorney Docket No. | 50304/113001 |
| | Serial No. | 10/595,126 |
| | Applicant | WAER et al. |
| | Filing Date | February 27, 2006 |
| | Group | 1626 |
| | IDS Filed | April 6, 2007 |

| | | | | | | |
|--|--------------|------------|-------------------|--|--|--|
| | 3,122,546 | 02-25-1964 | Osdene | | | |
| | 5,300,509 | 04-05-1994 | Block et al. | | | |
| | 5,500,428 | 03-19-1996 | Block et al. | | | |
| | 6,043,228 | 03-28-2000 | McMurray et al. | | | |
| | 2004/0102447 | 05-27-2004 | Bonnert et al. | | | |
| | 2005/0054653 | 03-10-2005 | Eisenbrand et al. | | | |
| | 2004/0077859 | 04-22-2004 | Waer et al. | | | |
| | 2006/0189620 | 8-24-2006 | Waer et al. | | | |
| | 2007/0043000 | 2-22-2007 | Waer et al. | | | |
| | 2006/0287314 | 12-21-2006 | Waer et al. | | | |
| | 2007/0004721 | 01-04-2007 | Waer et al. | | | |
| | 2007/0032477 | 02-08-2007 | Waer et al. | | | |
| | 6,946,465 | 09-20-2005 | Waer et al. | | | |
| | 5,641,783 | 06-24-1997 | Klein et al. | | | |
| | 3,162,635 | 12-1964 | Schroeder | | | |

| FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION | | | | | | |
|--|-----------------|---------------------------|--------------------------|-------|----------|----------------------|
| Examiner's Initials | Document Number | Publication or Issue Date | Country or Patent Office | Class | Subclass | Translation (Yes/No) |
| | CH 231,852 | 07-17-1944 | Switzerland | | | |
| | DD 267 495 | 05-03-1989 | Germany East | | | |
| | DE 19 21 308 | 01-07-1971 | Germany | | | |
| | DE 40 09 941 | 10-02-1991 | Germany | | | |
| | EP 0 108 890 | 05-23-1984 | EPO | | | |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | | |
|--|---|---|---|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) | Attorney Docket No. Serial No. Applicant Filing Date Group IDS Filed | 50304/113001 10/595,126 WAER et al. February 27, 2006 1626 April 6, 2007 |
| (37 C.F.R. § 1.98(b)) | | | |

| | | | | | | |
|--|--------------|------------|----------------|--|--|--|
| | EP 0 134 922 | 03-27-1985 | EPO | | | |
| | EP 0 185 259 | 06-25-1986 | EPO | | | |
| | EP 0 290 819 | 11-17-1988 | EPO | | | |
| | EP 0 362 645 | 4-11-1990 | EPO | | | |
| | EP 0 956 855 | 11-17-1999 | EPO | | | |
| | EP 1 479 682 | 11-24-2004 | EPO | | | |
| | EP 0 544 445 | 11-19-1992 | EPO | | | |
| | EP 0 574 906 | 12-22-1993 | EPO | | | |
| | GB 2 405 793 | 03-2005 | United Kingdom | | | |
| | GB 677,342 | 08-13-1952 | United Kingdom | | | |
| | GB 763,044 | 12-05-1956 | United Kingdom | | | |
| | GB 785,353 | 10-30-1957 | United Kingdom | | | |
| | WO 00/39129 | 07-06-2000 | WIPO | | | |
| | WO 00/45800 | 08-10-2000 | WIPO | | | |
| | WO 01/19825 | 03-22-2001 | WIPO | | | |
| | WO 01/21619 | 03-29-2001 | WIPO | | | |
| | WO 02/32507 | 04-25-2002 | WIPO | | | |
| | WO 03/062240 | 07-31-2003 | WIPO | | | |
| | WO 05/025574 | 03-24-2005 | WIPO | | | |
| | WO 94/11001 | 05-26-1994 | WIPO | | | |
| | WO 94/06431 | 03-31-1994 | WIPO | | | |
| | WO 95/31987 | 11-30-1995 | WIPO | | | |
| | WO 95/32203 | 11-30-1995 | WIPO | | | |
| | WO 98/04558 | 02-5-1998 | WIPO | | | |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | |
|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | Attorney Docket No. | 50304/113001 |
| | Serial No. | 10/595,126 |
| | Applicant | WAER et al. |
| | Filing Date | February 27, 2006 |
| | Group | 1626 |
| | IDS Filed | April 6, 2007 |

| | | | | | | |
|--|--------------|------------|------|--|--|--|
| | WO 98/08516 | 03-5-1998 | WIPO | | | |
| | WO 98/52948 | 11-26-1998 | WIPO | | | |
| | WO 04/104005 | 12-02-2004 | WIPO | | | |
| | WO 05/021003 | 03-10-2005 | WIPO | | | |
| | WO 05/039587 | 05-06-2005 | WIPO | | | |

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)

| | |
|--|---|
| | Baba et al., "Synergistic Antiviral Effects of Antiherpes Compounds and Human Leukocyte Interferon on Varicella-Zoster Virus in Vitro," <i>Antimicrob. Agents Chemother.</i> 25:515-517 (1984). |
| | Beers and Berkow, "The Merck Manual of Diagnosis and Therapy 17 th Edition," 1474-1476 (1999), <i>XP-002313611</i> . |
| | Beers and Berkow, "The Merck Manual of Diagnosis and Therapy 17 th Edition," 953-954 (1999), <i>XP-002313612</i> . |
| | Beilstein search, <i>XP-002324247</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 28:1015-1020 (1992), <i>XP-002296933</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 90:2631 (1957) <i>XP-002296934</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 93:2668 (1960) <i>XP-002296935</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 52:1403-1410 (2003) <i>XP-002296936</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 41:7811-788 (1995) <i>XP-002296937</i> . |
| | Beilstein Database, <i>Beilstein Institute For Organic Chemistry</i> 48:1255-1274 (1998) <i>XP-002296938</i> . |
| | Black et al., "Agents that Block TNF- α Synthesis or Activity," <i>Ann Rep. Med. Chem.</i> 32:241-250 (1997). |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | | |
|--|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | Attorney Docket No. | 50304/113001 |
| | | Serial No. | 10/595,126 |
| | | Applicant | WAER et al. |
| | | Filing Date | February 27, 2006 |
| | | Group | 1626 |
| | | IDS Filed | April 6, 2007 |

| | |
|---|---|
| | Boon, "Pteridines. Part IV.* Derivatives of 2:4-Diaminopteridine and Related Compounds," <i>J. Chem. Soc.</i> 2146-2158 (1957). |
| | Cairo, "Immunology Lecture #20 Transplantation," <i>Columbia University, [online]</i> (2003). |
| | Chantry "Emerging Drugs," 1:5-13 (1999). |
| | Chou and Talalay, "Quantitative Analysis of Dose-Effect Relationships: The Combined Effects of Multiple Drugs or Enzyme Inhibitors," <i>Adv. Enzyme Regul.</i> 22:27-55 (1984). |
| | Cottam et al., "Substituted Xanthines, Pteridinediones and Related Compounds as Potential Anti-Inflammatory Agents. Synthesis and Biological Evaluation of Inhibitors of Tumor Necrosis Factor .alpha.," <i>J. Med. Chem.</i> 39:2-9 (1996). |
| | Ellon et al., "Antagonists of Nucleic Acid Derivatives. VIII. Synergism in Combinations of Biochemically Related Antimetabolites," <i>J. Biol. Chem.</i> 208:477-488 (1954). |
| | Elliott et al., "Synthesis of N-10-Methyl-4-Thiofolic Acid and Related Compounds," <i>Journal of Medicinal Chemistry</i> 18:492-496 (1975). |
| | Froehlich et al., "Inhibition of Neuronal Nitric Oxide Synthase by 4-Amino Pteridine Derivatives: Structure-Activity Relationship of Antagonists of (6R)-5, 6, 7, 8-Tetrahydrobiopterin Cofactor," <i>Journal of Medicinal Chemistry</i> 48:4108-4121 (1999). |
| | Giori et al., "Reactivity of 3H-Pyrimido[5, 4-c] [1, 2, 5] Oxadiazin-3-One Towards Carbanions: Synthesis of Pteridine-2, 4-Diones," <i>J. Heterocyclic Chemistry</i> 23:1661-1665 (1986). |
| | Illei and Lipsky, "Novel, on-Antigen-Specific Therapeutic Approaches to Autoimmune/Inflammatory Diseases," <i>Current Opinion in Immunology</i> 12:712-718 (2000). |
| | Israel et al., "Pyrimidine Derivatives. VII. Some Condensed Derivatives of 2, 4, 5-Triamino-6-Methylthiopyrimidine," <i>Journal of Pharmaceutical Sciences</i> 54:1626-1632 (____). |
| | Kaldrikyan, M.A. et al., "Pteridine Derivatives. I. Synthesis of Some Substituted 6,7-Diarylpteridines," <i>Armianskii Khimicheskii Zhurnal</i> 29:337-341 (1976). |
| | Landauer and Rydon, "A Convenient Synthesis of Some 4-Substituted 5-Aminopyrimidines," <i>J. Chem. Soc.</i> 3721-3722 (1953). |
| | Landry, "Pharmacologie. Descibles vers l'indication Therapeutique," <i>Cours et Exercice</i> :177 (2003); XP-002313503. |
| | Lin et al., "Use of the Methylxanthine Derivative A802715 in Transplantation Immunology, I. Strong in Vitro Inhibitory Effects on CD28-Costimulated T Cell Activities," <i>Transplantation</i> 63:1813-1819 (1997). |
| | Lin et al., "Use of the Methylxanthine Derivative A802715 in Transplantation Immunology, II. In Vivo Experiments," <i>Transplantation</i> 63:1734-1738 (1997). |
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | |
|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | Attorney Docket No. | 50304/113001 |
| | Serial No. | 10/595,126 |
| | Applicant | WAER et al. |
| | Filing Date | February 27, 2006 |
| | Group | 1626 |
| | IDS Filed | April 6, 2007 |

| | |
|--|---|
| | Matter et al., "Structural Requirements for Inhibition of the Neuronal Nitric Oxide Synthase (NOS-I): 3D-QSAR Analysis of 4-Oxo- and 4-Amino-Pteridine-Based Inhibitors," <i>J. Med. Chem.</i> 45:2923-2941 (2002). |
| | Merz et al., "Synthesis of 7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidinopteridine and Novel Derivatives Free of Positional Isomers. Potent Inhibitors of cAMP-Specific Phosphodiesterase and of Malignant Tumor Cell Growth," <i>J. Med. Chem.</i> 41:4733-4743 (1998). |
| | Mohr et al., "Pteridines: Synthesis and Properties of 6-Thioxanthopterin and 7-Thioisoxanthopterin," <i>Helv. Chim. Acta</i> 75:2317-2326 (1992). |
| | Moreb and Zucali, "The Therapeutic Potential of Interleukin-1 and Tumor Necrosis Factor on Hematopoietic Stem Cells," <i>Leuk. Lymph.</i> 8:267-275 (1992). |
| | Murata et al., "A Facile Method for Regioselective 6,7-Disubstitution of Pteridine," <i>Heterocycles</i> 53:1259-1262 (2000). |
| | Nicolaus, B.J.R., "Symbiotic Approach to Drug Design", <i>Decision Making in Drug Research</i> , 173-186 (1983). |
| | Pfleiderer and Lohrmann, "Pteridine, XII: Synthese von 2-Amino-4-Alkoxy-Pteridinen," <i>Chem. Ber.</i> 94:12-18 (1961). |
| | Sato and Fukuya, "Studies on Pyrazines. Part 37. 'Synthesis of 6-Propionylpteridine-2,4 (1 <i>H</i> ,3 <i>H</i>)-dione and its 1-and/or 3-Methyl Derivatives from Marine Natural Products," <i>J. Chem. Soc., Perkin Trans.</i> 1:89-95 (2000). |
| | Spickett et al., "The Synthesis of Compounds With Potential Anti-Folic Acid Activity. Part I. 7-Amino- And 7-Hydroxy-Pteridines," <i>Journal of The chemical Society, Chemical Society. Letchworth</i> 2887-2891 (1954). |
| | Weinstock et al., "Pteridines. XII. Structure-Activity Relationships of Some Pteridine Diuretics," <i>J. Med. Chem.</i> 11:573-579 (1968). |
| | West, "Solid State Chemistry and its Applications," <i>Wiley</i> 358 & 365 (1988). |
| | Yao and Pfeleiderer, "Pteridines. Protection of Pteridines", <i>Helvetica Chimica Acta</i> , 86:1-12 (2003). |
| | Neilsen et al., "Unequivocal syntheses of 6-methyl- and 6-phenylisoxanthopterin" <i>J. Heterocyclic Chem.</i> , 24, pages 1621-1628 (1987) |
| | Taghavi-Moghadam et al., "A new, general, and regioselective method for the synthesis of 2, 6-disubstituted 4-aminopteridines", <i>Tetrahedron Lett.</i> , 38 (39), pages 6835-6836 (1997) |
| | Jackson et al., "6, 7-disubstituted 2, 4-diaminopteridines: novel inhibitors of <i>Pneumocystis carinii</i> and <i>Toxoplasma gondii</i> dihydrofolate reductase", <i>Antimicrobial Agents and Chemotherapy</i> , 40 (6), pages 1371-1375 (1996) |
| | Magnus et al. "Neural stem cells in inflammatory CNS diseases: mechanisms and therapy" <i>J. Cell. Mol. Med.</i> 2005, 9:303-319. |
| | Obach "Drug-drug interactions: an important negative attribute in drugs" <i>Drugs of Today</i> 2003, 39:301-338. |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |

| | | |
|--|---------------------|-------------------|
| SUBSTITUTE FORM PTO-1449 (MODIFIED) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) (37 C.F.R. § 1.98(b)) | Attorney Docket No. | 50304/113001 |
| | Serial No. | 10/595,126 |
| | Applicant | WAER et al. |
| | Filing Date | February 27, 2006 |
| | Group | 1626 |
| | IDS Filed | April 6, 2007 |

| | |
|--|--|
| | Cecil Textbook of Medicine, 20 th edition (1996), vol. 2, pp:2050-2057. |
| | Cecil Textbook of Medicine, 20 th edition (1996), vol. 2, pp:1992-1996. |
| | "FDA mulls drug to slow late-stage Alzheimer's" cnn.com 9/24/2003. |
| | Wikipedia entries for Antihistamine, Autoimmunity, List of autoimmune diseases, Lupus erythematosus, and Sjogren's syndrome, printed from http://en.wikipedia.org on December 28, 2006. |
| | Buu-Hoï et al., "Phthalonimides (1,3,4-Trioxo-1,2,3,4-tetrahydroisoquinolines) of Potential Biological Interest," J. Heretocycl. Chem., 1968, 5:545-546. |
| | Ganellin "Final Report on the Activities of the Medicinal Chemistry Section" [online] 14 January 2002 [retrieved on 2004-06-02] < www.iupac.org/divisions/VII/VII.M/VIIM-ReportDec2001.pdf > |
| | Abou-Hadeed et al. Pteridines (1996), 7(4) 113-122. |
| | Sugimoto et al. Pteridines (1997), 8(3), 188-194 |
| | Vinot Bulletin de la Societe Chimique France (1983), (9-10), Pt. 2), 2752-5. |
| | International Search Report, PCT/BE04/000124 |
| | International Preliminary Report on Patentability, PCT/BE04/000124 |
| | International Written Opinion, PCT/BE04/000124 |
| | European Communication, EP 04761485.4 |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant. | |